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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,506	12/19/2005	Andreas Meinke	SONN:085US/10512514	6550

32425 7590 08/21/2008
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EXAMINER	
OGUNBIYI, OLUWATOSIN A	
ART UNIT	**PAPER NUMBER**
1645	
MAIL DATE	**DELIVERY MODE**
08/21/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,506	MEINKE ET AL.	
	Examiner	Art Unit	
	OLUWATOSIN OGUNBIYI	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40,41,43,45,47-50 and 53-61* is/are pending in the application.

4a) Of the above claim(s) *53-56* is/are withdrawn from consideration.

5)☒ Claim(s) *40,41,43,45,47-50 and 58-61* is/are allowed.

6)☒ Claim(s) *57* is/are rejected.

7)☒ Claim(s) *57* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

The amendment filed 5/15/08 has been entered into the record. Claims 1-39, 42, 44, 46, 51-52 have been cancelled. Claims 40, 41, 43, 45, 47-50, 53-61 are pending. Claims 40, 41, 43, 45, 47-50 and 57-61 are under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Objections/Rejections Withdrawn

The objection of claims 45 and 51 under 37 CFR 1.75(c), as being of improper dependent form is withdrawn in view of the cancellation of claim 51.

The objections to claims 37, 38, 40 and 41 as being dependent on rejected claim 36 is withdrawn in view of the amendment to the claims to cancel claims 36-38.

The rejection of claim 51 under 35 U.S.C. 112, first paragraph is withdrawn in view of the cancellation of claim 51.

The rejection of claims 36, 39, 43, 45, 47, 48 and 51 under 35 U.S.C. 102(e) as being anticipated by Breton et al US 6,562,958 B1, May 13, 2003 filed June 4, 1999 as application

number 09/328,352, is withdrawn in view of the amendment to the claims and the cancellation of claims 36, 39 and 51.

The rejection of claims 36, 39, 43, 45 and 47-50 under 35 U.S.C. 103(a) as being unpatentable over Breton et al US 6,562,958 B1, May 13, 2003 filed June 4, 1999 as application number 09/328,352 in view of Meinke et al, WO 02/059148, Aug. 1 2002 is withdrawn in view of the amendment to the claims and the cancellation of claims 36, 39 and 51.

Rejections Maintained

The rejection of claims 43, 45, 47-50 and new claim 57 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an immunogenic formulation comprising an hyperimmune serum reactive antigen comprising an amino acid sequence consisting of SEQ ID NO: 91 or a fragment of least 8 contiguous amino acids of SEQ ID NO: 91, does not reasonably provide enablement for a pharmaceutical formulation or vaccine formulation comprising an hyperimmune serum reactive antigen comprising an amino acid sequence consisting of SEQ ID NO: 91 or a fragment of at least 8 contiguous amino acids of SEQ ID NO: 91 is maintained for reasons made of record in the previous office action mailed 1/15/08.

The nature of the invention is drawn to a pharmaceutical/vaccine formulation comprising an isolated hyperimmune serum reactive antigen comprising an amino acid sequence consisting of SEQ ID NO: 91 or a pharmaceutical/vaccine formulation comprising fragments of at least 8

contiguous amino acids of SEQ ID NO: 91. The instant specification contemplates pharmaceutical composition as a vaccine composition (p. 10 second to the last paragraph) and contemplates such compositions/medicaments as vaccine against *C. pneumoniae* infection (p. 4 third complete paragraph).

The specification teaches the identification of predicted immunogenic antigens e.g. SEQ ID NO: 91 and fragments of SEQ ID NO: 91 by using a screening method that uses serum from *Chlamydia* infected patients on a *C. pneumoniae* genomic expression library. The specification on p. 14 teaches that antibodies produced against *Chlamydia* by the human immune system and present in human sera are indicative of the *in vivo* expression of the antigenic proteins and their immunogenicity. The specification further predicts the T cell epitopes contained in SEQ ID NO: 91 (p. 48 example 5, table 51 SEQ ID NO: 91).

However, the specification does not correlate the immunogenicity of SEQ ID NO: 91 and predicted epitopes (fragments of SEQ ID NO: 91) with a protective immune response against *C. pneumoniae.* There is no challenge data in an animal model that provides evidence for a vaccine or prophylaxis (prevention) against infection by *C. pneumoniae*. The specification teaches that SEQ ID NO: 91 is immunogenic and predicts immunogenic T cell epitopes (or hyperimmune serum reactive) fragments of SEQ ID NO: 91; however immunogenicity does not predict a protective immune response. The specification in addition does not provide any guidance or direction as to any pharmaceutical property of compositions comprising an isolated hyperimmune serum-reactive antigen comprising an amino acid sequence consisting of SEQ ID NO: 91 or a fragment of at least 8 contiguous amino acids of SEQ ID NO: 91. As mentioned above, the specification only provides guidance and direction as to the immunogenicity of SEQ

ID NO: 91 and the prediction of its T cell epitopes. The instant specification clearly contemplates the use of any pharmaceutical composition of SEQ ID NO: 91 or fragments thereof as a vaccine.

Vaccines induce protection against infections by stimulating the development of long-lived effector cells and memory cells (Abbas et al. Cellular and Molecular Immunology 4th edition chapter 15 p. 360-362, 2000). Vaccines by definition trigger an immunoprotective response in the host vaccinated and mere antigenic response i.e. immunogenicity is insufficient. It is well recognized in the vaccine art, that it is unclear whether an antigen(s) derived from a pathogen will elicit protective immunity. Ellis, R.W. (Chapter 29 of "VACCINES" [PIotkin, S.A. et al. (eds) published by W. B. Saunders company (Philadelphia) in 1988, especially page 571, 2nd full paragraph] exemplifies this problem in the recitation that "The key to the problem (of vaccine development) is the identification of that protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies.... and thus protect the host against attack by the pathogen". In the instant case, the specification has not correlated the production of protective antibodies via active immunization with the claimed proteins with protection against *C. pneumoniae* in order to result in a vaccine or prophylactic treatment of an infection. Testing Chlamydia proteins identified by genomics and proteomics in an *in vivo* model where correlates of immunological protection can be examined provides a powerful combination for effective vaccine design (Thorpe et al. Vaccine vol. 25 p. 2252-2260, 2007). The art teaches that vaccine candidate antigens for *C. pneumoniae* are further tested in an animal model of infection to study induction of immunity and to correlate with protection from infection (Puolakkainen et al. Life Sciences vol. 322, p. 973-978 1999, Thorpe et al. Vaccine vol. 25 p. 2252-2260, 2007). The art also teaches that Chlamydia subunit vaccine candidates that have

demonstrated immunogenicity in vitro provide poor immunogenicity *in vivo* and consequently producing only partial protective immunity and antigen selection based solely on recognition by antibodies will likely not be suitable for inducing protective immunity against Chlamydia (Igietseme et al Expert Rev. Vaccines 2 (1), 129-146, 2003. See p. 135 columns 1 and 2). Thus, more guidance is needed to use the instant composition as a vaccine. It is impossible to predict the protective efficacy of SEQ ID NO: 91 or recited fragments based alone on the immunogenic data and the specification is devoid of data demonstrating the efficacy of SEQ ID NO: 91 or recited fragments as a vaccine in at least an experimental model of *C. pneumoniae* infection.

In view of the nature of the invention, lack of guidance presented in the specification and the absence of examples correlating the induction of a protective immune response to a pharmaceutical composition comprising a hyperimmune serum reactive antigen comprising SEQ ID NO: 91 or the recited fragments of the amino acid sequence of SEQ ID NO:91 with prevention of *C.pneumoniae* infection, the unpredictability as to whether said SEQ ID NO: 91 and a fragment thereof will induce a protective immune response, and the teachings of the vaccine art, undue experimentation will be required of the skilled artisan to practice the invention as claimed.

Applicants' can obviate the instant rejection by amending the claims to recite 'immunogenic composition' instead of pharmaceutical formulation or vaccine formulation.

Applicants' arguments and the Offices' response directed to vaccine formulation of the instantly claimed products:

Applicants urge that SEQ ID NO: 91 was identified as a hyperimmune serum reactive antigen and that T-cell epitopes were identified in the specification and that the epitopes are recognized by antibodies in human sera.

Applicants urge that the references cited above support the enablement for a vaccine. Applicants urge that these references show that protective immune responses against Chlamydia have been achieved with antigens identified through genomics and proteomics and that these references demonstrate *in vitro* and in animal models of Chlamydia infection and that using the teachings in the art, it would require no more than routine screening to make and use a vaccine formulation comprising the instant products.

Applicants' argument is carefully considered but is not persuasive. As mentioned above, an immunogenic response does not predict the protective efficacy of the instant products. Many antigens are immunogenic but it well known in the vaccine art that many immunogenic proteins do not go on to provide protection against infection. If protective efficacy were merely based on immunogenicity, then there will be no need to test immunogenic proteins for their protective efficacy. In the instant case, the specification has not correlated the production of protective antibodies via active immunization with the claimed proteins with (or any other immune response) protection against *C. pneumoniae* in order to result in a vaccine or prophylactic treatment of an infection. For any putative vaccine candidate including *C. pneumoniae* antigens, the art teaches that vaccine candidate antigens for *C. pneumoniae* are further tested in an animal model of infection to study induction of immunity and to correlate with protection from infection (Puolakkainen et al. Life Sciences vol. 322, p. 973-978 1999, Thorpe et al. Vaccine vol. 25 p. 2252-2260, 2007, Igietseme et al Expert Rev. Vaccines 2 (1), 129-146, 2003. See p. 135 columns

1 and 2). The teachings of the art however on how to screen for a vaccine, do not provide for the enablement of the instant product as a vaccine. The above references do not teach the instant antigen or fragments thereof and do not teach that SEQ ID NO: 91 is protective against *C. pneumoniae* infection. The teachings of the art are related to other proteins and not related to SEQ ID NO: 91. The protective efficacy of SEQ ID NO: 91 cannot be predicted from the teachings of the art concerning the protective efficacy whether partial or full of other *C. pneumoniae* antigens.

As to Applicants arguments that further research and development in the context of a pharmaceutical invention is expected and that the stage at which an invention in the pharmaceutical field becomes useful is well before it is ready to be administered is unpersuasive. The rejection above does not require evidence of clinical efficacy of the instant products in humans. It is well known for the vaccine art that antigens are usually tested for efficacy in animal models before proceeding further down the line to human trials. The instant specification has not even demonstrated the protective efficacy of the instant products in an animal model of *C. pneumoniae* infection and has not clearly demonstrated that the instant products are at the stage of usefulness as a vaccine in a model of *C. pneumoniae* infection. The specification at the time of filing should be enabled for a 'vaccine' formulation comprising the instant product. The vaccine art is highly complex and screening for a vaccine that would be protective is not routine experimentation and formulating a vaccine takes many years to accomplish. In the instant case, there is no guidance as to the protective efficacy of the instant product in at least an experimental model to provide some level of prediction as to the usefulness of the instant products as a vaccine. As clearly taught by the art, *Chlamydia* subunit vaccine candidates that have

demonstrated immunogenicity *in vitro* provide poor immunogenicity *in vivo* and consequently producing only partial protective immunity and antigen selection based solely on recognition by antibodies will likely not be suitable for inducing protective immunity against *Chlamydia* (Igietseme et al Expert Rev. Vaccines 2 (1), 129-146, 2003. See p. 135 columns 1 and 2). The instant specification does not even teach the protective efficacy of the instant products (whether partial or full immunity) and one of skill in the art cannot predict the efficacy of the instant products against *C. pneumoniae* infections or diseases caused by *C. pneumoniae*.

In view of the above, considerations, undue experimentation will be required of the skilled artisan to practice the invention as claimed. The recitation of 'an immunogenic formulation' instead of 'a vaccine formulation' would overcome the instant rejection.

New Objection Based on Amendment

1) Claim 57 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 57 is drawn to a vaccine formulation comprising the pharmaceutical composition of claim 43. The recitation of 'vaccine' is an intended use of the instant pharmaceutical composition of claim 43 and does not further structurally limit the composition of claim 43.

Status of Claims

Claims 40-41 and 58-61 are allowable. Claims 43, 45, 47, 48, 49, 50 and 57 are rejected. Claim 57 is objected to.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Oluwatosin Ogunbiyi whose telephone number is 571-272-9939. The examiner can generally be reached on M-F 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, either of the examiner's supervisors Shanon Foley (571-272-0898) or Robert Mondesi (571-272-0956) can be contacted.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Oluwatosin Ogunbiyi/

Examiner, Art Unit 1645

/Patricia A. Duffy/

Primary Examiner, Art Unit 1645